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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,091	04/23/2001	Athan Kuliopulos	18475-034 (NEMC-215)	4965

30623 7590 09/30/2003

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	19

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/841,091	KULIOPULOS ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *18,22-28,30 and 32-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17, 19-21, 29 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-34* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *06 February 2003* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *8,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, received 13 May 2002 and the Supplemental Information Disclosure Statement, received 28 June 2002, have been entered into the record as Papers 8 and 9, respectively. The Preliminary Amendment and Supplemental Preliminary Amendment have been entered as Papers 6 and 13. Applicant's election of Invention I (claims 1-17, 19-21, 29 and 31) in Paper No. 6 is acknowledged. In addition, Applicant elected the species: *Palmitate.*

Claims 18, 22-28, 30 and 32-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claims.

Claims 1-17, 19-21, 29 and 31 are under examination in the Instant Application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

URL's

The disclosure is objected to because it contains browser-executable code. This occurs,

for example, on p. 43, line 29. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only. See MPEP § 608.01 (p).

Appropriate correction is required.

Claim Objections/Rejections

Claims 3, 4, 8 and 19 are objected to for recited non-elected inventions (e.g., "ceramides" or "VIP" receptors).

Appropriate correction is required.

35 USC § 112, First Paragraph – Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-17, 19-21, 29 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the Specification, while being enabling for a pepducin constructed from the third intracellular loop of the PAR4 receptor, comprising the sequence TLAASG...RRY (SEQ ID NO: 9) and attached to a fatty acid such as palmitate, does not reasonably provide enablement for chimeric peptides comprising portions of G protein-coupled receptors other than PAR4, or of the extracellular domains of such G protein-coupled receptors, or of pepducins attached to hydrophobic moieties other than fatty acids such as palmitate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make the invention commensurate in scope with these claims.

Claims 1-17, 19-21, 29 and 31 are drawn to chimeric peptides comprising extracellular or intracellular portions of a G protein-coupled receptor coupled with hydrophobic moieties, provided the peptide-portion of the chimera does not comprise a native extracellular ligand. Dependent claims recite contiguous amino acids of 3-14 residues, a peptide comprising portions of transmembrane domain *TM5*, without the third intracellular loop, and chimeric pepducins constructed from the third intracellular loops of many other G protein-coupled receptors.

The specification discloses *pepducins* constructed from the third intracellular loop of the PAR4 receptor, comprising the sequence TLAASG...RRY (SEQ ID NO: 9) and attached to several fatty acids such as palmitate. Data is presented that demonstrate the pepducins constructed from this sequence of the third intracellular loop, and attached to hydrophobic moieties, interact intracellularly with the G -proteins associated with a specific receptor, generally inhibiting the expected cellular response. For example, pepducins acting at the platelet-aggregation receptors (PAR), inhibit inositol triphosphate production and subsequent platelet aggregation (Specification, Figures 4C and 4D).

However, a sufficient amount of direction or guidance is lacking in claims 1 Claims 1-17, 19-21, 29 and 31. The claims recite chimeric peptides comprising extracellular or intracellular portions of a G protein-coupled receptor coupled with hydrophobic moieties, provided the peptide-portion of the chimera does not comprise a native extracellular ligand. There are no definitive characteristics that distinguish the claimed peptides in terms of structure or function other than the exclusion of natural ligands. The numbers and types of proteins that can be formed from portions of G protein-coupled receptors is very large, probably variable in their

physiological effects, and largely untested (see the discussion in: Coughlin, et al, 2003, J. Clin. Invest., 111(1): 25-27).

Due to the large quantity of experimentation required to determine how to make all possible chimeric proteins that have the characteristics of being made from a G protein-coupled receptor but not comprising a natural ligand, the lack of direction or guidance in the specification regarding same (e.g., what sequences or structural requirements are necessary to maintain the functional characteristics of the polypeptides embraced by the claims), the lack of working examples to examples of all the claimed polypeptides, the state of the art showing the unpredictability of function based on structural similarity of proteins, and the breadth of the claims which embrace innumerable variants of *pepducins*, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

In summary, Claims 1-17, 19-21, 29 and 31 do not recite properties of the claimed pepducins in terms of precisely defined characteristics of the associated proteins and hydrophobic moieties, such that they can be distinguished from other proteins that may bind G proteins. Amending the claims to recite the disclosed sequences of the *i3* polypeptides, for example, would be remedial.

35 USC § 112, first paragraph – Written Description.

Claims 1-17, 19-21, 29 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application

was filed, had possession of the claimed invention.

Claims 1-17, 19-21, 29 and 31 are directed to the chimeric pepducin of claim 1, where the hydrophobic moiety is a lipid. "[A] lipid" can include, for example, steroids and phospholipids.

The specification teaches chimeric peptides comprising short peptide segments of G protein-coupled PAR receptors coupled to short linear fatty acids (for example: C_{10} or C_{16}). However, the specification does not teach functional or structural characteristics of polypeptides attached to lipids other than those similar to fatty acids such as palmitate. The description of several polypeptides attached to fatty acids is not adequate written description of an entire genus of functionally equivalent polypeptides attached to any lipid.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the pepducins referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptide/lipids, and therefore, would not know how to make or use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. *The product itself is required.* See *Fiers v. Revel*, 25 USPQ2d 1601 at

1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a polypeptide comprising the amino acid sequence of SEQ ID NO:9 and attached to a short linear fatty acid such as palmitate, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion:

Claims 1-17, 19-21, 29 and 31 are rejected for the reasons cited above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623. Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or

proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW

9/27/03

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER